TAB 24

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United States Department of Health Human Services

Testimony

Statement by
Janet Woodcock, M.D.
Director, Center for Drug Evaluation and Research, Food and Drug Administration, Department of Health and Human Services
on
FDA Regulates Prescription Drug Promotion
before the
The Senate Special Committee on Aging

INTRODUCTION

Mr. Chairman and Members of the Committee, I am Janet Woodcock, Director of the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA or the Agency).

Thank you for the opportunity to discuss how FDA regulates prescription drug promotion. I will present a brief background including how regulation in this area has evolved, the Agency's statutory and regulatory authority over promotional materials developed by manufacturers (sponsors) of products, how the Agency carries out these functions, various issues concerned with bringing such promotional materials before the public, recent FDA surveys conducted to assist us in evaluating the impact of prescription drug promotion to the public, and ongoing and future plans of the Agency with respect to these functions.

Helping all Americans make better informed health decisions is a top priority of the Agency. Previous research by FDA and other entities has documented that accurate consumer-directed or direct-to-consumer (DTC) prescription drug promotion can lead to significant increases in the detection of under-treated conditions like high blood pressure, diabetes, and depression, with consequent health benefits for Americans. FDA surveys in 1999 and 2002 showed that DTC advertising encouraged substantial numbers of patients to ask a doctor about a medical condition or illness of their own that they had not talked to a doctor about before. The surveys also showed that DTC advertising encouraged patients to obtain more health information from a physician or pharmacist. On balance, if this is happening as a result of DTC advertisements, this is very promising. I welcome the opportunity today to outline the approach FDA is taking in this area.

The Division of Drug Marketing, Advertising, and Communications (DDMAC), within CDER is responsible for regulating prescription drug promotion at FDA. DDMAC's mission is to protect the public health by helping to ensure that prescription drug information is truthful, balanced, and accurately communicated. This is accomplished through a comprehensive surveillance, enforcement and education program, and by fostering optimal communication of labeling and promotional information to both health care professionals and consumers.

KINDS OF MATERIALS REGULATED

FDA regulates advertisements and other promotional material, called "promotional labeling," disseminated by or on behalf of the advertised product's manufacturer, packer or distributor. Mostly, this means materials that the product's sponsor issues or places for publication, which are directed to consumers and patients, such as ads printed in magazines, journals and newspapers; ads broadcast over television, radio and telephone; brochures, letters and flyers sent through the mail; and videotapes, pharmacy counter displays, billboards, and patient compliance program materials. According to the October 2002 GAO report entitled, Prescription Drugs: FDA Oversight of Direct-to-Consumer Advertising Has Limitations, "Promotion to physicians accounted for more than 80 percent of all promotional spending by pharmaceutical companies in 2001." Therefore, the bulk of the Agency's time spent reviewing promotional material, is spent reviewing materials produced for promotion to health care professionals, such as detail aids used by manufacturer representatives, convention displays, file cards, booklets, and videotapes, which is distinct from advertising directed toward consumers.

TYPES OF ADVERTISEMENTS

Of the three different types of ads that product sponsors use to communicate with consumers, FDA regulates two of them; "product-claim" and "reminder" ads. The third type, "help-seeking" ads are not regulated by FDA.

"Product-claim" ads are regulated by FDA and are those ads which generally include both the name of a product and its use, or make a claim or representation about a prescription drug. Claims of drug benefits, such as safety and effectiveness, must be balanced with relevant disclosures of risks and limitations of efficacy. This balanced presentation of drug therapy is commonly referred to as "fair balance." In addition, when used in print ads, sponsors must provide a brief summary of risk information included in the product's FDA-approved labeling or, for broadcast "product-claim" ads, provide convenient access to the approved labeling. In our regulations, the phrase "adequate provision" is used to identify the convenient access option.

"Reminder" ads are regulated by FDA and are ads that may disclose the name of the product and certain specific descriptive information such as dosage form (i.e., tablet, capsule, or syrup) or price information, but they are not allowed to give the product's indication (use) or to make any claims or representations about the product. They specifically are not allowed for products with serious warnings (called "black box" warnings) in their labeling. The regulations specifically exempt "reminder" ads from the risk disclosure requirements because they were historically designed generally to remind health care professionals of a product's availability. Health care professionals presumably know both the name of a product and its use.

"Help-seeking" ads discuss a disease or condition and advise the audience to "see your doctor" for possible treatments. They need not include any risk information. Because no drug product is mentioned or implied, this type of ad is not considered to be a drug ad and is not regulated by FDA.

STATUTORY AND REGULATORY AUTHORITY

FDA regulates the manufacture, sale, and distribution of drugs in the United States under authority of the Federal Food, Drug, and Cosmetic (FD&C) Act (or the Act), which includes approval of prescription drug labeling that provides information about the use of a drug. Section 502(n) of the Act provides the Agency with authority to regulate prescription drug advertisements and the implementing regulations (Title 21, Code of Federal Regulations [CFR] section 202.1) which provide specifics about the content of such advertisements. Nothing in the law or regulations prohibits DTC promotion in any advertising medium even if the drug being advertised is a controlled substance. Also, the advertising provisions of the Act do not address the issues of pharmaceutical coverage by insurance companies or drug product price.

The regulations specify, among other things, that prescription drug advertisements cannot be false or misleading, cannot omit material facts, and must present a "fair balance" between benefit and risk

information. Further, for print advertisements, the regulations specify that every risk addressed in the product's approved labeling also must be disclosed in the brief summary. For broadcast advertisements, however, the regulations require ads to disclose the most significant risks that appear in the labeling. The regulations further require that broadcast advertisements either contain a brief summary of "all necessary information related to side effects and contraindications" or make adequate provision for dissemination of the product's FDA-approved labeling (and the risk information it contains) in connection with the ad.

FDA generally cannot require that prescription drug advertisements be reviewed and approved prior to their use. Prior FDA review of advertisements occurs only in very narrow circumstances, primarily for products receiving accelerated approvals. In other words, FDA's review of promotional materials is intended to occur post hoc - once the materials have appeared in public. Enforcement actions for advertising violations are generally intended to be taken post hoc as well. Most of FDA's enforcement actions request that sponsors stop using the violative materials. In some cases, FDA asks sponsors to run corrective advertisements or issue corrective letters to correct product misimpressions created by false, misleading, or unbalanced materials. To avoid this, the majority of sponsors voluntarily seek prior comment from FDA on draft broadcast ads for their products thereby reducing the likelihood that sponsors may face an enforcement action.

DEVELOPMENT OF REGULATION FOR CONSUMER-DIRECTED ADS

Prior to the early 1980s, prescription products were not promoted directly to consumers and patients. At that time, FDA's regulation of promotional drug material was limited to that which manufacturers prepared to present to physicians and other health care professionals. In the early 1980s, a few companies began advertising products directly to patient audiences (specifically, older people concerned about pneumonia and people taking prescription ibuprofen to treat arthritis pain). As questions and concerns directed to the Agency about such DTC promotion began to grow, FDA issued a policy statement on September 2, 1983, requesting a voluntary moratorium on DTC ads. The Agency needed time to study whether the current regulations developed in the 1960s for prescription drug advertising directed toward health care professionals provided sufficient safeguards to protect consumers when applied to DTC promotion. In addition, the Agency wanted to allow time for a dialogue among consumers, health professionals, and industry, and for interested parties to conduct research on aspects of consumer-oriented advertising. The industry complied with the request. In 1984, the University of Illinois and Stanford Research Institute jointly sponsored a symposium to discuss consumer-directed prescription drug advertising from a broad research and policy perspective.

In a September 9, 1985, Federal Register (FR) Notice (50 FR 36677), FDA concluded that the "current regulations governing prescription drug advertising provide sufficient safeguards to protect consumers," which lifted the voluntary moratorium.

During the early 1990s, sponsors increasingly used consumer print material (magazines, etc.) to advertise their products. The ads typically included a promotional message together with the brief summary of adverse effects, similar to that used in physician-directed ads. The brief summary statement, which frequently appears in small print using medical jargon, is not very consumer friendly.

In the 1990s, product sponsors also started using television advertisements in a limited fashion. Television advertisements were limited because of the extensive disclosure needed to fulfill the brief summary requirement, and FDA and industry did not believe that it was feasible to disseminate the product's approved labeling in connection with the ad. Therefore, it was believed that the brief summary was required. For example, one way to satisfy the brief summary requirement would be to scroll the brief summary on the screen, which would take a minute or more at a barely readable scrolling rate. By the mid-1990s, sponsors were placing "reminder" ads on television because these ads are not required to include a brief summary. Some of these ads were confusing to consumers who were not knowledgeable about the name and use for these products.

In response to increasing consumer demand for information and clarity, FDA issued an FR Notice on

August 16, 1995, announcing a public hearing to discuss several aspects of DTC advertising and a Notice for further comment on May 14, 1996, to clarify additional issues, including the brief summary requirement. Further, in light of changes in consumers' ability to get additional product information, FDA began to consider whether broadcast ads could be constructed to ensure access to product labeling information, the only alternative to including the brief summary requirement. FDA considered suggestions about providing access to multiple sources of product labeling as a means of satisfying the requirement that consumers have convenient access to FDA-approved labeling when manufacturers broadcast a "product-claim" ad.

In August 1997, FDA issued a draft guidance entitled, "Guidance for Industry: Consumer-Directed Broadcast Advertisements" (see Attachment A) that clarified the Agency's interpretation of the existing regulations. The Guidance described an approach for ensuring that audiences exposed to prescription drug advertisements on television and radio has convenient access to the advertised product's approved labeling. The proposed approach consisted of reference in the broadcast ad to four sources the consumer could use to obtain more detailed labeling information: a toll-free telephone number, a website address, a concurrently running print advertisement, and health care professionals. Following a comment period, and detailed review and consideration of the comments, FDA made only minor changes to the draft guidance, and issued it in final form in August 1999 (64 FR 43197, also found at: http://www.fda.gov/cder/guidance/1804fnl.htm).

In April 2001, FDA issued draft guidance for industry entitled, "Using FDA-Approved Patient Labeling in Consumer-Directed Print Advertisements." The draft guidance describes how FDA did not intend to object to the use of certain FDA-approved patient labeling to fulfill the brief summary requirement for prescription drug and biological product print advertisements directed toward consumers. FDA said it would not object to the use of FDA-approved patient labeling if such labeling were reprinted in full and comprehensively discussed in consumer-friendly language the product's most serious and most common risks. FDA believed that this labeling contained the information patients would likely find helpful in deciding whether to discuss with their health care provider the possible usefulness of the product for their own health care.

CDER's DDMAC OPERATIONS

Since 1997, DDMAC has been staffed with about 28-30 staff members. This has recently been increased to 40 staff members. Of the 40 staff members, 20 are primary reviewers and 5 are secondary reviewers (team leaders). The review staff currently has six review groups. Four are Professional Review Groups, each with two review teams, who review materials prepared for health care professionals. In addition, there is one Direct-to-Consumer Review Group consisting of two review teams and one research team; one Evidence Review Group; and a Policy and Enforcement Team. All report to the Division Director.

With the transfer of the therapeutic products from the Center for Biologics Evaluation and Research, (CBER), CDER has created a seventh review group within DDMAC to be officially transferred October 1, although the staff currently is at DDMAC in detail status. The Biologic Review Group, which consists of a team leader and three reviewers, will review the promotional materials for the products that are being transferred from CBER.

Under the post-marketing submission requirement, DDMAC received approximately 31,600 pieces of all categories of promotional material in 1999; 32,100 in 2000; 34,200 in 2001 and 36,700 in 2002. Although DDMAC is unable to thoroughly review every piece, certain materials are flagged for expedited review. These include materials that introduce newly approved products or products with new indications, which we identify as launch. These go to the Professional Review Groups and to the Direct-to-Consumer Review Group if consumer materials are part of the "launch" campaign. Also flagged for expedited review are TV and radio advertisements, which go to the Direct-to-Consumer Review Group. In addition to promotional materials that are submitted at the time of initial use, DDMAC reviews complaints about promotion from competitors, health care professionals, and consumers; promotional activities in the commercial exhibit halls of scientific meetings; promotional meetings; and evolving technology.

The total number of DTC broadcast advertisements (TV and radio) submitted to DDMAC in recent years was: 1999 - 293; 2000 - 443; 2001 - 376 and 2002 - 486. This includes both those advertisements that were proposed but not aired and those that were aired. Since January 1997, sponsors of 93 prescription drugs (see Attachment B) have aired "product-claim" and/or "reminder" advertisements on television or radio. A small number of prescription biological products also have been aired. It is important to note that DDMAC does not know how many different variations of the original advertisements have aired in broadcast media for these 93 drugs. Many of the products have been the subjects of multiple campaigns and many of the campaigns include different length "product-claim" commercials - variations of the initial commercial submitted to the Agency. It would be impossible for DDMAC to try to track the number of different broadcast advertisements that are aired. In addition, because "help-seeking" ads, if properly done, are not considered to be drug ads, most product sponsors do not send them to DDMAC. Thus, we have no measure of how many of them have been in the public domain.

DDMAC does not track the number of DTC print ads. Last year, however, DDMAC estimated the consumer pieces to be about one-sixth of the total, or about 6,000. It should be noted that these are not all DTC print and broadcast ads, but also consumer promotional pieces distributed by drug companies directly to consumers or through health care providers.

An Example of How the DTC Review Group Functions

DDMAC uses a group meeting to discuss proposed promotional pieces and decide on our response to the company. A typical meeting to review a new proposal for a drug that already has been advertised in a broadcast medium includes a DTC review team and group leader, someone from one of the professional review groups, a social scientist, and a regulatory counsel, also from DDMAC's staff. Drugs that are new products, have new indications, are first in a class to have broadcast advertisements, or are being advertised in a broadcast medium for the first time have more extensive reviews.

Almost all companies send new proposed DTC broadcast concepts to DDMAC for comments in advance of use, although companies are under no obligation to follow DDMAC's advice. Consequently, DDMAC generally does not see the final broadcast ad before the company submits it as part of its post-marketing requirements at the time the ad is first aired on TV or radio. DDMAC instituted the group review process for proposals in an effort to help ensure that DDMAC provide consistent advice to companies across product classes, and over time.

Current Regulatory Tools

As stated previously, unless sponsors voluntarily submit their draft materials for comment before use, DDMAC sees the materials at the same time as the public. DDMAC's options to address promotional materials that are false or misleading are:

- Untitled letters -notices of violations issued to sponsors directing that they discontinue use of the violative false or misleading advertising materials
- Warning Letters - issued to sponsors for more serious violations, such as those possibly posing serious health risks to the public
- Injunctions and consent decrees
- Referrals for criminal investigation or prosecution
- Seizures

FDA has moved toward a risk-based enforcement strategy designed to achieve effective deterrence through use of Warning Letters and untitled letters that are more clearly designed to serve as a basis for further enforcement action. Under a directive issued to FDA by the Department of Health and

Human Services in November 2001, all Warning Letters and untitled letters that originate within FDA, including DDMAC letters, must be reviewed and cleared by the Agency's Office of the Chief Counsel (OCC) before issuance. OCC review focuses on ensuing that the correct legal violation has been cited, that the violation is substantiated by the facts, and that enforcement action is legally sustainable if the violation continues. Under this system, a firm that receives a DDMAC letter is on notice that OCC has already determined that enforcement action based on the cited violation stands a relatively high likelihood of succeeding in court. Put another way, FDA now uses Warning Letters to presage enforcement action, not substitute for it. Moreover, firms that commit repeated violations face a much stronger basis for further enforcement action. The Agency acknowledges that in some instances, this may result in longer review times, however, OCC and DDMAC work together to minimize delays and have agreed to expedite the review of certain letters by setting a goal of 15 working days for completing such reviews.

Criteria Used When Issuing an Untitled or Warning Letter

Untitled letters are used for less serious violations than Warning Letters. Such violations may include overstating the effectiveness of the advertised drug product, suggesting a broader range of conditions than the drug was approved for, or making misleading claims because of inadequate context or lack of balancing risk information. Warning Letters address more serious violations including serious safety or health risks and/or repetitive violative conduct which, if not promptly and adequately corrected, could lead to additional enforcement actions without further notice from FDA. Warning Letters generally result in the company disseminating a remedial message to correct the violative ad.

Educational Programs for Industry

DDMAC aims to increase voluntary compliance by industry through educational programs. These programs include outreach, website postings, guidances, and advisory comments.

Outreach Programs: FDA staff participates in many panel discussions and presentations for groups including industry, law firms, consultants to industry, and marketing and advertising agencies. These programs are intended to increase these groups' understanding of the regulations relating to promotion of prescription drugs so that industry can better comply.

Website Postings: CDER posts on its website all Warning Letters and Untitled Letters and the cited promotional materials. Industry has noted that these letters serve as useful examples of violations that FDA has acted against and helps them understand what type of promotion is unacceptable.

Guidances: FDA publishes guidances in areas for which industry seeks clarification. An example is the guidance on broadcast advertisement published in August 1999, following on the draft guidance published in August 1997. Guidances help industry understand FDA's current thinking and how to comply with the regulations.

Advisory Comments: Although there is no requirement, for most drugs, that companies submit proposed promotional materials BEFORE their initial use, companies often request DDMAC's review and comments on proposed materials. We provide this service so that companies can ensure that their materials are in compliance with the regulations.

ENFORCEMENT RELATED TO DTC PROMOTION

Since August 1997, for broadcast advertisements, FDA has issued:

- 45 untitled (or "Notice of Violation") letters on "product-claim" broadcast ads. Such letters request that the violative promotion be stopped immediately. Product sponsors virtually always comply immediately with this request.

- 3 Warning Letters on broadcast ads. This is a higher-level enforcement action, and requests that a remedial campaign be conducted by the company to correct the misimpressions left by the ad.
- 13 untitled letters on purported reminder broadcast ads.
- 3 untitled letters on purported "help-seeking" broadcast ads.

Most of the violations cited were because the ad overstated or guaranteed the product's efficacy, expanded the indication or the patient population approved for treatment, or minimized the risks of the product, through either inadequate presentation or omission of information.

Since August 1997, for print advertisements, the Agency has issued:

- 54 untitled letters that addressed DTC print ads or other promotional materials, including purported "reminder" and "help-seeking" materials.
- 2 Warning Letters: one for a specific DTC print ad and one that included a DTC print ad as part of an overall misleading campaign.

Generally, the violations for "product-claim" print ads were similar to those cited above. Nearly all "reminder" ad violations were the result of representations about the product that triggered the need for full disclosure of benefits and risks. "Help-seeking" ad violations were due to a particular product being suggested in the message. FDA cannot determine how many specific advertisements serve as the denominator for assessing how many have resulted in enforcement action compared with those that have not.

FDA'S DTC PROMOTION RESEARCH

A number of groups, including FDA, have been conducting research on DTC promotion to learn about its effects on consumers and physicians. As part of its commitment to examine the effect of DTC promotion on public health, FDA has conducted three national telephone surveys of U.S. adults to ask their views on DTC promotion of prescription drugs and its effects on the patient-physician relationship. One consumer survey was conducted in the spring of 1999 and again in the spring of 2002. FDA has only released the preliminary results of the 2002 consumer and physician surveys and is currently working on the final report which is expected to be released some time in the fall of 2003. FDA is planning a public meeting to present this information and to give other organizations and individuals an opportunity to present their research to FDA. Specifics about this meeting will be announced in the Federal Register at a later date.

TWO FDA CONSUMER SURVEYS ON DTC PROMOTION

In the two consumer surveys, FDA gave special attention to surveying adults who had recently visited a physician (within the last three months). Participants were asked questions measuring the influence of DTC advertising on attitudes toward prescription drugs, health-related behavior, and on aspects of the doctor-patient relationship. The preliminary results from these two consumer studies show:

- Among respondents who had seen a doctor with the past three months and remembered seeing an ad for a prescription drug, approximately half in 1999 and approximately 40 percent in 2002 said that an advertisement for a prescription drug had caused them to seek more information, for example, about the drug and their health.
- Among those respondents who indicated that a DTC ad had caused them to search for more

information in 2002, 61 percent reported they were searching for information about side effects.

- More than a quarter (27 percent) of survey respondents in 1999 and 18 percent in 2002 who had seen a doctor in the last three months said that an ad for a prescription drug had caused them to ask a doctor about a medical condition or illness that they had not talked to a doctor about before.
- In both 1999 and 2002, the most frequently reported reasons for visiting a doctor are the presence of a previous condition, the need for a checkup, or that the respondent had not been feeling well. Less than 7 percent of respondents report that they visited their doctor because of something they read or saw, or because of an ad for a prescription drug.
- Forty-two percent of respondents in 2002 agreed strongly or somewhat agree that DTC ads make it seem as though the drug will work for everyone.

The results of the two consumer surveys need additional analysis but indicate that DTC may serve as stimulus for consumers to seek more information about their health and the drug product including the risks associated with the use of the drug.

PRELIMINARY RESULTS OF FDA's 2002 SURVEY OF PHYSICIANS

Highlights of the preliminary results of FDA's survey of 500 physicians in the U.S. about DTC promotion include:

- Many physicians believe that DTC advertising can play a positive role in their interactions with their patients. For example, most agreed that because their patients saw a DTC ad, he or she asked more thoughtful questions.
- Some physicians thought the ads made their patients more aware of possible treatments.
- Many physicians thought that DTC ads made their patients more involved in their health care.
- Physicians felt they had to provide additional information to patients beyond what the patients retained from the DTC ad. About 75 percent believed that DTC ads cause patients to think the drug works better than it did, and many physicians felt some pressure to prescribe something when patients mentioned DTC ads.
- Forty percent of physicians believe that patients understood well the possible risks and negative effects of an advertised drug from the DTC ad alone.
- Eight percent of physicians felt very pressured and 20 percent felt somewhat pressured to prescribe the specific brand name drug when the patient asked the physician to do so. Most physicians suggested alternative courses of action.

The physician survey is an important tool to consider when doing the evaluation of the impact of DTC advertising on public health because of the role of the physician as the "learned intermediary." The patient does not select the drug for self-use but the decision is made by the physician in consultation with the patient. The results of the physician survey are preliminary but indicate that DTC advertising, when done correctly, can serve positive public health functions such as increasing patient awareness of diseases that can be treated, and prompting thoughtful discussions with physicians that result in needed treatments being prescribed. Often, the treatment that was prescribed was not the drug the patient saw advertised. Physicians in this survey indicate that they appeared comfortable in not necessarily prescribing the advertised drug for reasons including: that a different drug was more appropriate, the drug was not right for the patient, the drug has side effects of which the patient was not aware, and/or a less expensive drug was available. Two concerns that physicians expressed are

that DTC advertising causes patients to think that the drug works better than it did and that patients did not understand very well the possible risks of the advertised drug.

FUTURE AGENCY ACTIVITIES CONCERNING DTC ADVERTISING

FDA is committed to ensuring that its DTC advertising policies promote truthful and non-misleading advertising that helps to better inform consumers about their health and health care choices and prevents potential misconceptions about benefits and risks of the advertised treatment. Two concerns expressed by some physicians in FDA's survey, relate to overstatement of the product's efficacy and inadequate conveyance of risk information, and are two of the most common violations cited in the letters that FDA issues to pharmaceutical companies about DTC ads. FDA will continue to review DTC ads closely to ensure that essential information is communicated as clearly as possible, as outlined in our current policies. In addition, FDA will continue its comprehensive evaluation of DTC advertising and its impact on public health and FDA's policies and guidances.

In sum, prescription drug advertising can provide consumers with important information about new prescriptions and new indications for existing prescription drugs, as well as information about symptoms of treatable illnesses and other conditions. Done properly, prescription drug advertising can assist consumers in taking a pro-active role in improving their health. However, to be of value, these advertisements must not be false and misleading. As a result, FDA continues to closely monitor DTC advertising to help ensure that this promotional activity is accurate and balanced. FDA will complete evaluation of its own research and that of other groups to help ensure that FDA's policies in regulating DTC advertising are optimal. To this end, the Agency is planning a public meeting in the fall for a full discussion of the known research.

This concludes my remarks, Mr. Chairman. I will be glad to answer any questions you may have.

Last Revised: May 19, 2003

TAB 25

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Mr. Vincent DeStefano
Associate Director, Regulatory Affairs
Novartis
560 Morris Avenue
Summit, New Jersey 07901-1312

RE: **NDA#s 17-874, 20-501** Transderm Scop (scopolamine) Transdermal Therapeutic System
MACMIS# 10972

Dear Mr. DeStefano:

This letter notifies you that, through routine monitoring and surveillance, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has identified a professional journal advertisement (ID 0928-00) for Transderm Scop (scopolamine) Transdermal Therapeutic System that is misleading and thus in violation of the Federal Food, Drug, and Cosmetic Act and applicable regulations.

Specifically, DDMAC objects to the following:

Your journal advertisement is misleading because it promotes an unapproved dosing regimen for Transderm Scop. The journal advertisement is entitled, "Long Lasting Prevention of PONV" (post operative nausea and vomiting), and in the second bulleted statement instructs physicians to "apply patch behind ear 1 to 4 hours prior to surgery."

This dosing regimen is inconsistent with the instructions in the Dosage and Administration section of the approved product labeling (PI). The PI states that, to prevent post-operative nausea and vomiting, the Transderm Scop patch should be applied the evening before scheduled surgery, except in the case of cesarean section (for cesarean section, the patch should be applied 1 hour prior to surgery to minimize the drug exposure to the newborn). Furthermore, although it appears that there is some circulating scopolamine at 4 hours or even sooner, the Clinical Pharmacology section of the PI indicates that peak levels are not obtained, on average, until 24 hours.

FDA's determination of the appropriate dosing and dosage regimen for an indicated use of a drug is often based on a complex balance of factors related to the efficacy of the product, adverse event and toxicity risks, and considerations of administration. FDA is not aware of any data to support the dosing recommendation in the ad. Because peak levels of scopalamine are not obtained, on average, until 24 hours after administration, applying the patch just 4 hours before surgery will likely decrease the expected effectiveness of Transderm Scop.

Additionally, our records indicate that this advertisement was not submitted to DDMAC. FDA regulations at 21 CFR §314.81(b)(3)(i) require that sponsors submit all advertising at the time of initial publication.

To address these objections, DDMAC recommends that Novartis do the following:

1. Immediately discontinue the use of this journal advertisement, as well as any other promotional material and practices with the same or similar messages.

2. Respond to this letter within 10 days. Your response should include a statement of your intent to comply with the above, a list of all promotional materials with the same or similar issues, and your methods for discontinuing these promotional materials.

If you have any questions or comments, please contact Dr. Lisa Stockbridge by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-42, rm. 8B-45, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds you that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #10972 in addition to the NDA number.

Sincerely,

{See appended electronic signature page}

Lisa L. Stockbridge, Ph.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Lisa Stockbridge
12/3/02 10:54:29 AM

168879

Long Lasting Prevention of PONV*†1,2

Transderm Scōp® average price

Cost per hour **$0.19**

Cost per 24 hours **$4.62**

- Just $0.19 per hour to prevent PONV for 24 hours
- Convenient and easy — apply patch behind ear 1 to 4 hours prior to surgery
- Most frequently reported adverse events were dry mouth (29%) and dizziness (12%)[1]

Stock Transderm Scōp in your pharmacy. Now available in convenient 24-patch Multipack — NDC0067-4346-24.

TRANSDERM SCŌP®
scopolamine 1.5 mg "THE NAUSEA PREVENTION PATCH"

*Based on labeled frequency of dosing.
†PONV=postoperative nausea and vomiting.

Available by prescription only. Transderm Scōp should not be prescribed for children, or for patients with glaucoma, difficulty in urinating, or an allergy to scopolamine or other belladonna alkaloids. Exercise special care when prescribing Transderm Scōp for the elderly. In postoperative nausea and vomiting clinical studies, the most commonly reported adverse events were dry mouth (29%) and dizziness (12%). While using this product, one should not drive, operate dangerous machinery, or do other things that require alertness. One should not use alcohol.

Please see accompanying Brief Summary of complete Prescribing Information.

To learn more about Transderm Scōp, visit www.transderm scop.com

References: 1. Transderm Scop [package insert]. Summit, NJ: Novartis Consumer Health Inc. 2. *Physicians' Desk Reference*®. 54th ed. Montvale, NJ: Medical Economics Inc. 2000. 3. *2000 Drug Topics Red Book*®. Vol 20 No 4. Montvale, NJ: Medical Economics, Inc. 2001.

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0928-00